American Journal of Medical Genetics 63:426–427 (1996)

A New Case of Klippel-Trenaunay-Weber (KTW) Syndrome: Evidence of Autosomal Dominant Inheritance

José M. Ceballos-Quintal, Doris Pinto-Escalante, and Ileana Castillo-Zapata

Centro de Investigaciones Regionales "Dr. Hideyo Noguchi," Laboratorio de Genética, Universidad Autónoma de Yucatán, Yucatán, México

Most cases of KTW syndrome are sporadic. However, in a few, other family members have some clinical manifestations of the syndrome, and an autosomal dominant mode of inheritance has been suggested. In this paper we present a family with an affected child who has large skin hemangiomata, overgrowth of the right leg, and severe heart defects. Her mother has a large capillary hemangioma on the left side of back and has developed severe varicosities in both lower extremities. The maternal grandmother developed severe varicosities in her legs at a young age. The clinical signs found in the mother and maternal grandmother represent a milder phenotype and might be explained as variable expressivity of the syndrome. The family tree supports autosomal dominant inheritance.

KEY WORDS: Klippel-Trenaunay-Weber syndrome, autosomal dominant inheritance, angioosteohypertrophy syndrome, birth defect, congenital malformations

INTRODUCTION

Klippel-Trenaunay-Weber syndrome was first described in 1900 by Klippel and Trenaunay [Klippel and Trenaunay, 1900]. The main findings of this condition include large hemangiomata in the skin and hypertrophy of one or more limbs. Varicose veins are commonly seen, and additional vascular abnormalities can occasionally be present (arteriovenous fistula, hemangiomas of internal organs, lymphangiomatous anomalies, telangiectasia and lymphectasia). Hypertrophy of bones and soft tissues are observed in the overgrown limbs. Other defects are infrequently described in digits, skin, head, eyes, and viscera [Jones, 1990; Lindenauer, 1965; McKusick, 1994; Viljoen, 1988; Viljoen et al., 1987].

Most cases are sporadic; however, in a few families other close relatives have some of the common features of this syndrome [Lindenauer, 1965; Norwood, 1964], and an autosomal dominant mode of inheritance with variable expression has been suggested [McKusick, 1994].

A family with a child having KTW syndrome is presented in this paper. The mother and maternal grandmother of the child have some clinical features of this condition.

CLINICAL REPORT

The patient is a 3-year-old girl with fairly normal psychomotor development, and weight and height between the 5th and 10th percentile (Fig. 1). She is the only child of a healthy, young, nonconsanguineous couple. She was born after an uneventful full-term pregnancy with a normal delivery. Physical examination at birth revealed weight of 2,900 g, length of 50 cm, and head circumference of 34 cm. Hypertrophy of the right lower limb was noted with the right leg being 1 cm longer than the left with a greater rate of growth postnatally. Capillary hemangiomata were present on the back, the right and lower third of the left gluteal area, the right leg, and in the genital fold. The skin was not warm over the hemangiomata. In addition, congenital fractures were found in the right femur, tibia and fibula, and several heart defects (patent ductus arteriosus, auricular septal defect, prolapsed tricuspid valve, pulmonic stenosis) were also present at birth. The hemangiomata have not changed and the difference between the legs is now 3 cm. Soft tissue masses were not found.

The mother had normal development, and has a large capillary hemangioma of 13 × 14 cm on the left side of back (Fig. 2). In addition she has developed severe varicosities in both legs and has no clinical or radiological signs of limb hypertrophy.

The maternal grandmother developed severe varicosities in both legs at a young age, and no hemangiomata were present, but we could not perform a physical examination.

Received for publication May 8, 1995; revision received December 18, 1995.

Address reprint requests to Dra. Doris Pinto-Escalante, CIR. "Dr. Hideyo Noguchi". Univ. Aut. De Yuc., 59 No. 490 x Av. Itzáes, Mérida 97000, Yucatán, México.

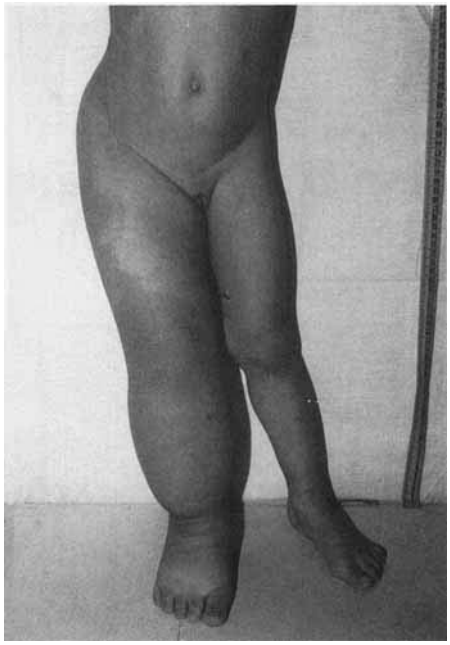

Fig. 1. Legs of the proposita at 3 years of age.

Fig. 2. The hemangioma of the mother.

DISCUSSION

The proband described herein has the association of large hemangiomata in the skin and limb hypertrophy which are the main clinical findings of KTW syndrome. Additionally, the occurrence of clinical signs of the syndrome in the mother and maternal grandmother of the index case is compatible with autosomal dominant inheritance with variable expressivity, as previously suggested by others [Norwood, 1964; Lindenauer, 1965]. The cardiovascular anomalies found in the index case are an infrequent finding in the KTW syndrome, and this may be random association, or could represent additional manifestations of vascular abnormalities in this syndrome.

Some other conditions with congenital overgrowth and hemangiomata have been described. Included in the differential diagnosis of KTW syndrome are 1) Proteus syndrome, characterized by subcutaneous hamartomas (including hemangiomas, lymphangiomas, and lipomas), overgrowth of any body structure and additional malformations; and 2) Maffuci's syndrome, with enchondromas present in addition to hemangiomas. Neither diagnosis fits the present family. Other cases with hemangiomata, such as Sturge-Weber syndrome and familial cavernous angioma, have the angiomata in different sites, namely the face and central nervous system [Jones, 1990; McKusick, 1994].

In conclusion, the findings in this family support an interpretation of autosomal dominant inheritance of this syndrome. A milder phenotype in the mother and grandmother can be explained as an example of variable expressivity, common in autosomal dominant disorders. The previously published sporadic cases of KTW syndrome could represent new dominant mutations. Determining the mode of inheritance of this syndrome to identify for proper counselling of families concerning recurrence risks in future pregnancies.

ACKNOWLEDGMENTS

We thank QFB Jorge Canto Herrera for his assistance in photography of the index case.

REFERENCES

Jones KL (1990): "Atlas de Malformaciones Congénitas." Editorial Interamericana McGraw-Hill, México, pp 506–507.

Klippel M, Trenaunay P (1900): Du naveus variqueux osteohypertrophique. Arch Gen Med 185:641.

Lindenauer SM (1965): The Klippel-Trenaunay-Weber syndrome: Varicosity, hypertrophy and hemangioma with no arteriovenous fistula. Ann Surg 162:303–314.

McKusick VA (1994): "Mendelian Inheritance in Man. Catalogs of Autosomal Dominant, Autosomal Recessive, and X-linked Phenotypes." Baltimore: Johns Hopkins University Press, p 848.

Norwood OT, Everett MD (1964): Cardiac failure due to endocrine dependent hemangiomas. Arch Derm 89:759–760.

Viljoen DL (1988): Klippel-Trenaunay-Weber syndrome (angioosteohypertrophy syndrome). J Med Genet 25:250–252.

Viljoen D, Saxe N, Pearn J, Beighton P (1987): The cutaneous manifestations of the Klippel-Trenaunay-Weber syndrome. Clin Exp Derm 12:12–17.